



# VIRCHOWS ARCHIV

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Abstracts



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immunostained with CD8 (C8/144B-Dako), FOXP3 (EP340-Epitomics), PD-L1 (SP263-Ventana), and CD163 (EP324-Epitomics). CD8, FOXP3, and CD163 expressions were separately evaluated in intratumoural(IT) and stromal(S) areas. PD-L1 expression was also individually considered in neoplastic cells (NC) and tumour-infiltrating-lymphocytes (TIL).

**Results:** All patients were female. Mean age was 52.7 (32-84) and mean survival was 48.3 months (3.4-83.7). There was a significant positive correlation between the expressions of each of the four antibodies ( $p<0.01$ ). Among the histological subtypes, higher expressions of CD8 (IT), FOXP3 (IT&S), PD-L1 (NC), and CD163 (IT&S) were found in lymphocyte-predominant breast carcinomas ( $p<0.05$ ). Expressions of CD8, FOXP3, and CD163 (IT&S), and PD-L1 (TIL) were negatively related to angio and lymphatic invasion ( $p<0.01$ ). Perineural invasion was more frequent in the cases with lower CD8 (S) and FOXP3 (IT&S) and higher PD-L1 (TIL) expressions ( $p<0.01$ ). pT stage was reversely related to CD8 (S) and PD-L1 (TIL), however, it had a positive association with PD-L1 (NC) and CD163 (IT) ( $p<0.01$ ). Lower expressions of FOXP3 (IT&S), PD-L1 (TIL), and CD163 (IT) were observed to be related with exitus ( $p<0.01$ ). Local recurrence was negatively associated with CD8 (S), FOXP3 (IT), PD-L1 (TIL), CD163 (S) ( $p<0.01$ ). Expressions of CD8 (S), FOXP3 (IT&S), PD-L1 (NC&TIL), and CD163 (IT&S) were lower in the cases with distant metastasis ( $p<0.01$ ).

**Conclusion:** TIME is an important prognostic parameter and a potential therapeutic marker. CD8, FOXP3, PD-L1, and CD163 antibodies are useful to consider TIME and to predict prognosis in TNBC.

#### PS-01-057

##### Relationship of Her2/neu and oestrogen receptor changes in local metastases compared with primary tumour in breast cancer patients with equivocal (2+) Her2/neu expression level in primary tumour

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**Background & Objectives:** Differences in the expression of biomarkers in primary tumour tissue and metastases and the relationships of such differences in breast cancer patients are not clear until now. Objective: to reveal the relationship of estrogen receptor (ER) and Her2/neu changes in locoregional metastases compared with primary tumour in the group of breast cancer patients with equivocal Her2/neu expression level (2+).

**Methods:** 19 samples of primary tumour (Her2/neu expression 2+) and corresponding metastases were stained immunohistochemically with anti-ER (1D5, Dako) and anti-Her2/neu (4B5, Ventana) antibodies. Primary tumour samples were additionally analysed using SISH technology (Ventana). Staining results were evaluated using Allred score and ASCO/CAP 2013 guideline. Frequencies of Her2/neu and ER expression changes were compared using Fisher's exact probability test.

**Results:** Her2/neu expression level was lower in metastases than in the primary tumour in 16 cases (84.2%, 95% CI 59.5-95.8%) and higher – in 1 case out of 19 (5.3%, 95% CI 0.3-28.1%) ( $p<0.001$ ). Her2/neu-statuses of primary tumour and metastases were the same in 84.2% (95% CI 59.5-95.8%) of cases. Among 16 cases with decreased Her2/neu expression level in metastases we registered 9 cases with increase and 2 cases with decrease of ER expression level ( $p=0.023$ ).

**Conclusion:** We found simultaneous decrease of Her2/neu expression level, maintenance of Her2/neu-status and increase of ER expression level in local metastases compared with primary tumour of breast cancer in the cases with equivocal (2+) Her2/neu expression level in the primary tumour.

#### PS-01-058

##### Androgen receptor expression as a possible prognostic marker in male breast cancer

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**Background & Objectives:** Male breast cancer (MBC) is a rare condition representing the 0.5-1% of all breast cancer cases. In contrast to female breast cancer (FBC), relatively little is known about MBC. Most MBCs are luminal A or B types, whereas basal-like and HER2 enriched types are rare. This distribution is clearly different compared to FBC, pointing to possible important differences in carcinogenesis. Increasing data deal with the role of the androgen receptor (AR) as a marker of prognosis in FBC, with contrasting results. Since the androgen – AR signalling exerts actions on key events during prostate carcinogenesis, the aim of the present study was to evaluate the role of AR in MBC.

**Methods:** 23 males with a diagnosis of invasive breast cancer were selected. Clinico-pathological data were collected. AR expression was measured by immunohistochemistry (SP107, Ventana Medical Systems; Ventana BenchMark AutoStainer). Pathological variables were compared by Spearman's rank correlation coefficient. Moreover, the Kaplan–Meier method and log-rank test were used to explore the impact of AR expression on disease free survival (DFS).

**Results:** 16 out of 23 patients (70%) displayed and increase of AR expression with the increase of Progesterone Receptor (PgR) expression ( $\rho = 0.484$ ;  $p = 0.019$ ). Instead, 7 out of 23 patients (30%) with low levels of PgR displayed high levels of AR with a potential advantage in terms of DFS ( $p=0.081$ ).

**Conclusion:** These preliminary data suggest a possible prognostic role of AR in MBC. Forthcoming molecular analysis will shed light to unknown underlying mechanisms.

#### PS-01-059

##### Expressed cartilaginous and osseous metaplasia in breast cancer: histological and immunohistochemical aspects

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**Background & Objectives:** The course of the breast cancer (BC) depends on the differentiation of the tumour, immunophenotype of the neoplastic cells and the qualitative and quantitative characteristics of the tumour microenvironment. Moreover, the expressed secondary changes significantly influence on the progression of the malignant process in the mammary gland. We present the case of the invasive breast cancer (non-specific type) of the right breast in a 64-year-old woman with the features of the expressed rare type of metaplasia.

**Methods:** Morphogenesis and immunophenotype of the tumour were studied by using the histological (H&E) and immunohistochemical (CKpan, Er, Pr, PRL, Her2neu, Ki-67, EGFR, MPO, GPA, CD3, CD79, CD68, OPN and OSN) methods.

**Results:** The high-grade invasive cancer of non-specific type with the expressed cartilaginous and osseous metaplasia was diagnosed. Immunohistochemical study revealed the strong expression for CKpan, OPN, OSN, PRL, moderate-EGFR, weak-Er, negative-Pr and Her2neu in the cancer tissue; Ki-67 expression was found in 7% of tumour cells. In the areas of osseous and cartilaginous tissue, the accumulation of single CD3, CD79α vs CD68 positive cells with MPO and GPA positive cells was revealed which confirms the formation of red bone marrow in the centre of metaplasia.

**Conclusion:** This clinical observation presents the case of the breast cancer, where the immunophenotype of cancer cells is the indicator of the possible osteo/chondrogenesis with the formation of bone marrow. Timely determination of the expression peculiarities of immunohistochemical markers in cartilaginous and osseous

metaplasia makes it possible to predict the course of the oncological disease and its metastasis.

#### PS-01-060

##### Clinicopathological and immunohistochemical characterisation of adenoid cystic carcinoma of the breast diagnosed in a single Institution

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**Background & Objectives:** Adenoid cystic carcinoma (ACC) is a rare but distinct breast neoplasm resembling its counterpart in other organs. It is architecturally heterogeneous and composed of a dual cell population, expressing epithelial and myoepithelial markers. Nevertheless, there is some controversy in the literature regarding its immunohistochemical profile. The aim of this study was to characterise the clinical, histological and immunohistochemical features of ACC cases diagnosed in our Institution.

**Methods:** A retrospective analysis of patients with ACC of the breast in our Institution was carried out. Twelve cases were included (1987-2018). Histological pattern and Nottingham Histological Grade (NG) were evaluated. Immunohistochemistry with hormonal receptors (estrogen-ER and progesterone-PR), human epidermal growth factor receptor type 2 (HER2), p63, calponin, vimentin, S100, smooth muscle actin (SMA), CK7, CAM5.2, CK5/6, CD117 and CK14 was performed for each case.

**Results:** Mean tumour size was 2.2cm. NG was 1(n=7), 2(n=3) and 3(n=1). Six cases were predominantly tubular/cribriform and six had solid/basaloid areas. 75% were triple-negative. All cases stained for CK7 and vimentin and eleven for CD117 and p63, each. Remaining markers stained variably. In predominantly tubular/cribriform tumours CK7, CD117, p63 and vimentin clearly identified two different cell populations. In solid tumours there was more epithelial-myoepithelial staining overlap with these markers. NG3 case was the only with nodal and distant metastasis.

**Conclusion:** ACC has good prognosis and characteristic histological and immunohistochemical features. Nevertheless, in tumours with predominantly solid/less differentiated areas there is more histological and immunohistochemical heterogeneity, which makes the differential diagnosis with other basaloid salivary gland-like carcinomas of the breast more challenging.

#### PS-01-061

##### Analysis of clinical-pathological data with impact on overall survival (OS) in male breast carcinoma (MBC): an international multi-Institutional study of 217 cases

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**Background & Objectives:** Male breast carcinoma is still inadequately characterised and data regarding the impact of different prognostic parameters are limited due to the small number of cases compared to female counterpart. The objective of this study is to evaluate clinical-pathological parameters in correlation with OS in male breast carcinoma.

**Methods:** All men diagnosed with invasive breast carcinoma in 6 international Institutions (1999- 2015) were identified by searching laboratory databases. Parameters analysed were the followings: age, tumour size, histological tumour type and grade, molecular biomarkers (ER, PR, ki-67, HER2), AR status, treatment and length of OS (months).

**Results:** 217 cases, with a mean age of 62y (range: 18- 85), right breast localization (52.53%), NST histological type (86.18%), G2 histological grade (55.4%), T2 (54.41%), N+ (65.89%) and Luminal A molecular subtype (85.29%) were identified. 5-year OS was 67.2% and 10-year OS was 48.5%. OS was 92.7% at 5 years and 73.8% at 10 years (in axillary lymph node negative cases) while OS was 59.7% at 5 year and 41.3% at 10 years in axillary positive male cancers (p=0.003).

#### PS-01-062

##### Higher tumour cell proliferation in breast cancer of the young

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**Background & Objectives:** Breast cancer (BC) in adolescents and young adults (AYAs; 15-49 years) is associated with aggressive tumour features. We aimed to investigate tumour cell proliferation in AYAs.

**Methods:** The proliferation marker Ki67 was analysed by immunohistochemistry on FFPE TMA-slides from two population based cohorts: One AYA series (n=355) and one series of patients aged 50-69 (n=546). mRNA data from METABRIC and TCGA (n=2283) was used to investigate gene expression signatures reflecting tumour proliferation.

**Results:** The AYAs demonstrated higher Ki67 levels compared to BC patients  $\geq 50$  years (median Ki67 10.4% and 7.0%, respectively;  $P<0.0005$ ). Higher Ki67 levels were found among AYAs  $<40$  years compared to those 40-49 years (median Ki67: 16.0% and 9.0%, respectively;  $P=0.009$ ). High levels of Ki67 among AYAs were associated with high histologic grade, ER and PR negativity, larger tumour diameter, and shorter survival (all  $P<0.0005$ ). When adjusting for tumour size, histologic grade and lymph node status, Ki67 maintained independent prognostic impact, also among ER positive AYA tumours. Higher mRNA proliferation scores in the young, and associations between high scores and shorter survival, validated our results (all  $P<0.0005$ ).

**Conclusion:** BC of the young demonstrate higher tumour cell proliferation compared to older patients, and higher proliferation associate with aggressive tumour features and reduced survival among AYA patients. This might contribute to the more aggressive breast cancers observed in the young.

#### PS-01-063

##### Is breast cancer different in women younger than 40 years old?

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